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Date: February 6, 2007

Name: Margaret M. Gliaos

Signature: 
Gibbons, Del Deo, Dolan, Griffinger & Vecchione, P.C.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: A.P. Kozokowski Confirmation No.: 7176
Serial No.: 10/783,801
Filed: February 20, 2004 Customer No.: 26345
Title: Synthesis of 4- α -Arylepicatechins
Examiner: Toafiq A. Solola
TC/A.U.: 1626

REQUEST FOR A CERTIFICATE OF CORRECTION

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The error in the filing date of Serial No. 09/655,360 is a Patent Office printing error. The correct Domestic Priority date of 09/05/2000 is shown on the Corrected Filing Receipt attached as Exhibit 1.

The error in step (b) of Claim 2 is a Patent Office error. See the May 15, 2006 Response to Restriction Requirement where in step (b) of Claim 38 (Claim 2 of the '014 patent) "the C-4 position" is identified.

A copy of the Restriction Requirement is attached as Exhibit 2 (see Claim 38 on page 4).

Since these are Patent Office, errors no fee should be due.

CORRESPONDENCE AND FEES

In the event that any fees are required, authorization is hereby given to charge Deposit Account No. 03-3839. Please address all correspondence to Intellectual Property Docket Administrator, Gibbons, Del Deo, Dolan, Griffinger & Vecchione, One Riverfront Plaza, Newark, NJ 07102-5497.

Should there be any questions or other matters that may be resolved by a telephone call, the Examiner is invited to contact the undersigned attorney at the number below.

February 6, 2007

Respectfully submitted,

Gibbons, Del Deo, Dolan, Griffinger & Vecchione

By Margaret B. Kelley
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EXHIBIT 1



UNITED STATES PATENT AND TRADEMARK OFFICE

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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/783,801	02/20/2004	1626	770	5677-215		7	1

Clifford Chance US LLP
 200 Park Avenue
 New York, NY 10166-0153

CONFIRMATION NO. 7176
CORRECTED FILING RECEIPT
OC000000014878088
 OC000000014878088

Date Mailed: 01/05/2005

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

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Assignment For Published Patent Application

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Domestic Priority data as claimed by applicant

This application is a DIV of 10/214,830 08/08/2002 PAT 6,720,432
 which is a DIV of 09/655,360 09/05/2000 PAT 6,476,241

Foreign Applications

If Required, Foreign Filing License Granted: 10/08/2004

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US10/783,801**

Projected Publication Date: 01/20/2005

Non-Publication Request: No

Early Publication Request: No

Title

Synthesis of 4alpha-arylepicatechins

Preliminary Class

549

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Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15**

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EXHIBIT 2

CERTIFICATE OF MAILING/FAX TRANSMISSION

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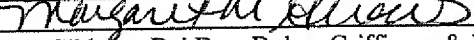
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___ submitted via EFSWEB filing.

Date: May 15, 2006

Name: Margaret M. Gliaros

Signature: 
Gibbons, Del Deo, Dolan, Griffinger & Vecchione, P.C.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: A.P. Kozokowski Confirmation No.: 7176
Serial No.: 10/783,901
Filed: February 20, 2004 Customer No.: 26345
Title: Synthesis of 4- α -Arylepicatechins
Examiner: Toafiq A. Solola
TC/A.U.: 1626

RESPONSE TO RESTRICTION REQUIREMENT

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is submitted in response to the Restriction Requirement mailed April 14, 2006. A
response is due May 16, 2006.

Amendment to the claims begins on page 2.

The Restriction Requirement begins on page 10.

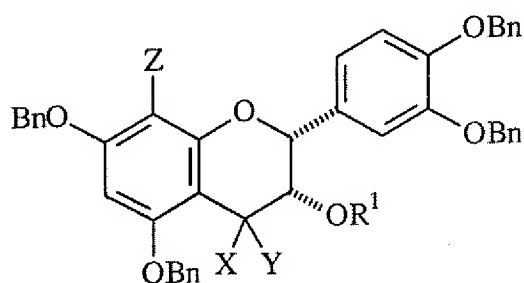
Remarks begin on page 11.

LISTING OF THE CLAIMS:

This listing of claims replaces all prior versions and listings of claims in this application.

Claims 1-21 (canceled)

Claim 22 (previously presented) A compound having the formula:



wherein R¹ is a silyl protecting group or a benzyl protecting group, wherein X and Y are independently hydrogen or hydroxy, and wherein Z is a hydrogen.

Claims 23-24 (canceled)

Claim 25 (previously presented) The compound of Claim 22, wherein R¹ is the silyl protecting group.

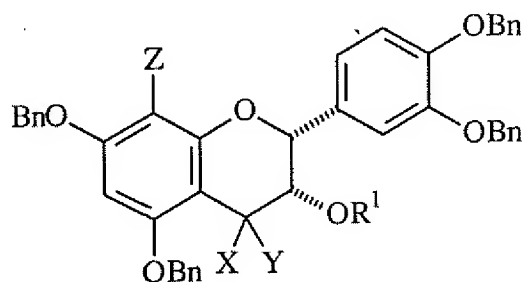
Claim 26 (previously presented) The compound of Claim 25, wherein the silyl group is a *tert*-butyldimethylsilyl group.

Claim 27 (previously presented) The compound of Claim 22, wherein R¹ is the benzyl protecting group.

Claims 28-30 (canceled)

Claim 31 (previously presented) The compound of Claim 22, which is 3, 5, 7, 3', 4'-penta-O-benzyl-4-hydroxyepicatechin or 5, 7, 3', 4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxyepicatechin.

Claim 32 (previously presented) A compound having the formula:



wherein R¹ is a silyl protecting group or a benzyl protecting group, wherein X and Y together are oxygen, and wherein Z is hydrogen.

Claim 33 (currently amended) The compound of Claim 32, wherein [[R1]] R¹ is the silyl protecting group.

Claim 34 (previously presented) The compound of Claim 33, wherein the silyl group is a *tert*-butyldimethylsilyl group.

Claim 35 (currently amended) The compound of Claim 32, wherein [[R1]] R¹ is the benzyl protecting group.

Claim 36 (currently amended) The compound of Claim 32, which is ~~(2R,3S)-~~
~~3,5,7,3',4'-pentakis-(benzyloxy) flavan-4-one~~ (2R,3S)-3,5,7,3',4'-pentakis-(benzyloxy)flavan-4-
one or ~~(2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-[(*tert*-butyldimethylsilyl)oxy]flavan-4-one~~ (2R,3S)-
5,7,3',4'-tetra-O-benzyl-3-O-[(*tert*-butyldimethylsilyl)oxy]flavan-4-one.

Claim 37 (previously presented) A process for preparing epicatechin-(4 α ,8)-catechin dimer, which process comprise the steps of:

- (a) protecting the 3-hydroxyl group of 5,7,3',4'-tetra-O-benzyl-epicatechin with a benzyl protecting group to form 3,5,7,3',4'-penta-O-benzyl-epicatechin;
- (b) oxidizing the C-4 position of the epicatechin of step (a) to form 3,5,7,3',4'-penta-O-benzyl-4-hydroxy-epicatechin;

- (c) oxidizing the C-4 hydroxyl group of the epicatechin of step (b) to form (2R,3S)-3,5,7,3',4'-penta-O-benzyl-4-ketone-epicatechin;
- (d) adding *tert*-butyl lithium to 3,5,7,3',4'-penta-O-benzyl-8-bromo-catechin to form a catechin-lithium reagent;
- (e) adding the epicatechin from step (c) to the catechin-lithium reagent from step (d) to form 3,5,7,3',4'-penta-O-benzyl-4-hydroxy-epicatechin-(4 α ,8)-(3,5,7,3',4'-penta-O-benzyl)-catechin dimer;
- (f) reducing the C-4 hydroxyl group of the dimer from step (e) to form 3,5,7,3',4'-penta-O-benzyl-epicatechin-(4 α ,8)-(3,5,7,3',4'-penta-O-benzyl)-catechin dimer; and
- (g) replacing the benzyl groups of the dimer of step (f) with hydrogen to form the epicatechin-(4 α ,8)-catechin dimer

Claim 38 (previously presented) A process for preparing 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-4 α ,8-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-catechin dimer comprises the steps of:

- (a) protecting the C-3 hydroxyl group of 5,7,3',4'-tetra-O-benzylepicatechin with a *tert*-butyldimethylsilyl group to form 5,7,3',4'-tetra-O-benzyl-C-3-O-(*tert*-butyldimethylsilyl)-epicatechin;
- (b) oxidizing the C-4 position of the epicatechin from step (a) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin;
- (c) oxidizing the C-4 hydroxyl group of the epicatechin from step (b) to form (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-ketone-epicatechin;
- (d) adding *tert*-butyllithium to 5,7,3',4'-tetra-O-benzyl-8-bromo-3-O-(*tert*-butyldimethylsilyl)-catechin to form a catechin-lithium reagent;

(e) adding the epicatechin from step (c) to the catechin-lithium reagent from step (d) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin-4 α ,8-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-catechin dimer;

(f) reducing the C-4 hydroxyl group of the dimer from step (e) to form the 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-4 α ,8-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)]-catechin dimer.

Claim 39 (previously presented) A process for preparing an epicatechin-(4 α ,8)-(3-O-acyl)-catechin dimer comprises the steps of:

(a) protecting the C-3 hydroxyl group of 5,7,3',4'-tetra-O-benzyl-epicatechin with a *tert*-butyldimethylsilyl group to form 5,7,3',4'-tetra-O-benzyl-C-3-O-(*tert*-butyldimethylsilyl)-epicatechin;

(b) oxidizing the C-4 position of the epicatechin from step (a) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin;

(c) oxidizing the C-4 hydroxyl group of the epicatechin from step (b) to form (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-*tert*-butyldimethylsilyl-4-ketone-epicatechin;

(d) adding *tert*-butyl lithium to 5,7,3',4'-tetra-O-benzyl-8-bromo-3-O-(*tert*-butyldimethylsilyl) catechin to form a catechin-lithium reagent;

(e) adding the epicatechin from step (c) to the catechin-lithium reagent from step (d) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin-(4 α ,8)-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)]-catechin dimer;

(f) reducing the C-4 hydroxyl group of the dimer from step (e) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-(4 α ,8)-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)]-catechin dimer;

(g) replacing the *tert*-butyldimethylsilyl protecting groups of the dimer of step (f) with hydrogen to form 5,7,3',4'-tetra-O-benzyl-epicatechin-(4 α ,8)-(tetra-O-benzyl-catechin)-dimer;

(h) acylating the 3-OH position of the dimer of step (g) with an activated acid or an acid chloride to form a 5,7,3',4'-tetra-O-benzyl-epicatechin-(4 α ,8)-[5,7,3',4'-tetra-O-benzyl-(3-O-acyl) catechin]-dimer; and

(i) replacing the benzyl protecting groups of the dimer from step (h) with hydrogen to form the epicatechin -(4 α ,8)-(3-O-acyl)-catechin dimer.

Claim 40 (previously presented) The process of Claim 37, wherein the protecting step (a) is carried out with benzyl bromide in the presence of sodium hydride; wherein the oxidizing step (b) is carried out with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and 4-(dimethylamino) pyridine; wherein the oxidizing step (c) is carried out with tetrapropylammonium perruthenate and N-methylmorpholine-N-oxide; wherein the reducing step (f) is carried out with tri-*n*-butyltin hydride followed by trifluoroacetic acid; and wherein the benzyl replacement step (g) is carried out by hydrogenation in the presence of palladium hydroxide on carbon.

Claim 41 (previously presented) The process of Claim 38, wherein the protecting step (a) is carried out with *tert*-butyldimethylsilyl chloride; wherein the oxidizing step (b) is carried out with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and 4-(dimethylamino) pyridine; wherein the oxidizing step (c) is carried out with N-methylmorpholine-N-oxide and tetrapropylammonium perruthenate; and wherein the reducing step (f) is carried out with tri-*n*-butyltin hydride and trifluoroacetic acid.

Claim 42 (previously presented) The process of Claim 39, wherein the protecting step (a) is carried out with *tert*-butyldimethylsilyl chloride; wherein the oxidizing step (b) is carried out with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and 4-(dimethylamino) pyridine; wherein the oxidizing step (c) is carried out with N-methylmorpholine-N-oxide and terapropylammonium perruthenate; wherein the reducing step (f) is carried out with tri-*n*-butyltin hydride and trifluoroacetic acid; wherein the *tert*-butyldimethylsilyl replacement step (g) is carried out with hydrofluoric acid; and wherein the benzyl replacement step (i) is carried out by hydrogenation in the presence of palladium hydroxide on carbon.

Claim 43 (previously presented) The process of Claim 39, wherein the acid is selected from group consisting of caffeic, coumaric, ferulic, and sinapic acid.

Claim 44 (previously presented) The process of Claim 39, wherein the acid is a hydroxy-protected acid selected from the group consisting of cinnamic acid, gallic acid, and hydroxybenzoic acid.

Claim 45 (previously presented) The process of Claim 39, wherein the acid is tri-*O*-benzylgallic acid and the epicatechin-(4 α , 8)-(3-*O*-acyl)-catechin dimer is epicatechin-4 α ,8-(3-*O*-galloyl)-catechin dimer.

Claim 46 (currently amended) A protected dimer selected from the group consisting of 5,7,3',4'-tetra-*O*-benzyl-3-*O*-(*tert*-butyldimethylsilyl)-epicatechin-(4 α ,8)-[5,7,3',4'-tetra-*O*-benzyl-3-*O*-(*tert*-butyldimethylsilyl)]-catechin; 3,5,7,3',4'-penta-*O*-benzyl-epicatechin-(4 α ,8)-(3,5,7,3',4'-penta-*O*-benzyl-catechin); and 5,7,3',4'-tetra-*O*-benzyl-epicatechin-(4 α ,8)-(5,7,3',4'-tetra-*O*-benzyl-catechin).

Claim 47 (previously presented) A protected epicatechin-(4 α ,8)-catechin dimer having a 4-hydroxy group selected from the group consisting of 5,7,3',4'-tetra-*O*-benzyl-3-*O*-

(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin-(4 α ,8)-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)catechin] and 3,5,7,3',4'-penta-O-benzyl-4-hydroxy-epicatechin-(4 α ,8)-(penta-O-benzyl-catechin).

Claim 48 (previously presented) A derivatized 5,7,3',4'-tetra-O-benzyl-epicatechin-(4 α ,8)-(5,7,3',4'-tetra-O-benzyl-catechin) dimer having at least one 3-O-acyl group.

Claim 49 (previously presented) The dimer of Claim 48, wherein the 3-O-acyl group is introduced using an acid selected from the group consisting of caffeic acid, coumaric, ferulic acid, and sinapic acid as a derivatizing agent.

Claim 50 (previously presented) The dimer of Claim 48 which is epicatechin-(4 α ,8)-[(3-O-acyl)-catechin].

Claim 51 (previously presented) The dimer of Claim 48, wherein the 3-O-acyl group is introduced using a hydroxy-protected acid selected from the group consisting of cinnamic acid, gallic acid, and hydroxy-benzoic acid as a derivatizing agent.

Claim 52 (previously presented) The dimer of Claim 51, wherein the 3-O-acyl group is a 3-O-(3,4,5-tri-O-benzylgalloyl) group.

Claim 53 (previously presented) The dimer of Claim 52 which is epicatechin-(4 α ,8)-[(3-O-galloyl)-catechin].

Claim 54 (previously presented) An epicatechin-(4 α ,8)-catechin dimer.

RESTRICTION REQUIREMENT

Restriction has been required as follows:

Group I - Claims 22, 25-27, 31-36 directed to tetra-O-benzyl-protected monomers having a benzyl or a silyl protecting group at C-3, e.g., 3,5,7,3',4'-penta-O-benzyl-3-O-benzyl-4-hydroxy-epicatechin or 5,7,3',4'-tetra-O-benzyl-3-O-*tert*-butyl-dimethylsilyl-4-hydroxy-epicatechin, (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-[(*tert*-butyldimethylsilyl)oxy]-flavan-4-one, or (2R,3S)-3,5,7,3',4'-pentakis(benzyloxy)-flavan-4-one;

Group II - Claims 37 and 40 directed to a process for making an epicatechin dimer, specifically an EC-(4 α ,8)-C dimer;

Group III - Claims 38 and 41 directed to a process for making the compounds of Group I;

Group IV - Claims 39 and 42-45 directed to a process for making an EC-3-O-acyl dimer, e.g., EC-(4 α ,8)-3-O-galloyl-C dimer;

Group V - Claims 46-47 directed to specific protected dimers; e.g., 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-EC-(4 α ,8)-5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-C or 3,5,7,3',4'-penta-O-benzyl-(4 α ,8)-3,5,7,3',4'-penta-O-benzyl-C, or 5,7,3',4'-tetra-O-benzyl-EC-(4 α ,8)-tetra-O-benzyl-C;

Group VI - Claims 48-53 directed to a tetra-O-benzyl-protected-(4 α ,8)-dimer having at least one 3-O-acyl group, e.g., EC-(4 α ,8)-[3-O-galloyl]-C]; and

Group VII - Claim 54 directed to an EC-(4 α ,8)-C dimer.

REMARKS

Applicants elect with traverse the claims of Group II, i.e., Claims 37 and 40 directed to a process for making an epicatechin-(4 α ,8)-catechin dimer. It is respectfully requested that the claim of Group VII, which is directed to the same dimer, i.e., an epicatechin-4 α ,8-catechin dimer, be examined at the same time. It would appear that a separate search would not be required or, if required, would not be unduly time consuming.

It is respectfully pointed out that the claims of Group III, i.e., Claims 38 and 44, are not directed to a process for making the compounds of Group I. The compounds of Group I are protected monomers, whereas the compounds made by the process of Claims 38 and 41 are protected dimers.

It is also respectfully pointed out that most of the claims do not cover a large number of compounds. Claims 37, 40, and 54 are all directed to one specific dimer, i.e., an EC-(4 α ,8)-C dimer.

CORRESPONDENCE AND FEES

In the event that any fees are required, authorization is hereby given to charge Deposit Account No. 03-3839. Please address all correspondence to Intellectual Property Docket Administrator, Gibbons, Del Deo, Dolan, Griffinger & Vecchione, One Riverfront Plaza, Newark, NJ 07102-5497.

Ser. No. 10/783,801
Gibbons 105942-53920

Should there be any questions or other matters that may be resolved by a telephone call,
the Examiner is invited to contact the undersigned attorney at the number below.

May 15, 2006

Respectfully submitted,

Gibbons, Del Deo, Dolan, Griffinger & Vecchione

By Margaret B. Kelley
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<p>(To be used for all correspondence after initial filing)</p> <p>Total Number of Pages in This Submission 12</p>		<p>Application Number 10/783,901</p> <p>Filing Date 2/20/04</p> <p>First Named Inventor A.P. Kozakowski</p> <p>Art Unit 1820</p> <p>Examiner Name Teahq A. Bolek</p> <p>Attorney Docket Number 106942-53020</p>	
<p><input type="checkbox"/> Fee Transmittal Form</p> <p><input type="checkbox"/> Fee Attached</p> <p><input type="checkbox"/> Amendment/Reply</p> <p><input type="checkbox"/> After Final</p> <p><input type="checkbox"/> Affidavits/Declaration(s)</p> <p><input type="checkbox"/> Extension of Time Request</p> <p><input type="checkbox"/> Express Abandonment Request</p> <p><input type="checkbox"/> Information Disclosure Statement</p> <p><input type="checkbox"/> Certified Copy of Priority Document(s)</p> <p><input type="checkbox"/> Reply to Missing Parts/Incomplete Application</p> <p><input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.62 or 1.63</p>		<p><input type="checkbox"/> Drawings(s)</p> <p><input type="checkbox"/> Licensing-related Papers</p> <p><input type="checkbox"/> Petition</p> <p><input type="checkbox"/> Petition to Convert to a Provisional Application</p> <p><input type="checkbox"/> Power of Attorney, Revocation</p> <p><input type="checkbox"/> Change of Correspondence Address</p> <p><input type="checkbox"/> Terminal Disclaimer</p> <p><input type="checkbox"/> Request for Refund</p> <p><input type="checkbox"/> CD, Number of CD(s) _____</p> <p><input type="checkbox"/> Landscape Table on CD</p> <p>Remarks _____</p>	
<p><input type="checkbox"/> After Allowance Communication to TC</p> <p><input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences</p> <p><input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)</p> <p><input type="checkbox"/> Proprietary Information</p> <p><input type="checkbox"/> Status Letter</p> <p><input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):</p> <p>Response to Restriction Requirement</p>		<p>SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT</p> <p>Firm Name Gibbons, Dol Deo, Dolan, Griffinger & Vecchione, P.C.</p> <p>Signature <i>Margaret B. Kelley</i></p> <p>Printed name Margaret B. Kelley</p> <p>Date May 15, 2006</p> <p>Reg. No. 39,181</p>	

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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 7,126,014 B2

DATED : 10/24/2006

INVENTOR(S) : Kozikowski, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

at (62) delete "Sep. 5, 2001" and insert

-- filed on Sep. 5, 2000 --

in Claim 2, at column 21, line 20, rewrite "the C-3 position" as

-- the C-4 position --

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Newark, New Jersey 07102-5496

PATENT NO. 7,126,014 B2

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